discrepancies turn out to be mainly aberrations which are correctable in their wider context. Over the years death certification has improved with advances in medicine. More information is given and it is more precise. We should tackle administrative weaknesses such as failure of pathologists to state explicitly causes of death, failure to update after necropsy, and relegation of completion to junior doctors without instruction. Over the past 140 years these records (the results of everyday experience of doctors) have contributed a great deal to our knowledge of the health of the nation and to medical research. Of course, there is a continuous need to study their flaws—especially as part of practical research—as was done in the papers by the study group of the Royal College of Physicians. I trust that these papers will be read constructively, otherwise they may have a negative effect, the best becoming the enemy of the good.

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¹ Birkelo, C C, *et al*, *Journal of the American Medical Association*, 1947, **133**, 359.

² Heasman, M A, and Lipworth, L, in *Studies on Medical and Population Subjects No 20*, p 133. London, HMSO, 1966.

³ Waldron, H A, and Vickerstaff, L, *Intimations of Quality*. London, Nuffield Provincial Hospitals Trust, 1977.

⁴ Barraclough, B, *et al*, *British Journal of Psychiatry*, 1974, **125**, 355.

⁵ Adelstein, A M, and White, G, in *Population Trends* 6, p 7. London, HMSO, 1976.

⁶ Inman, W H W, and Adelstein, A M, *Lancet*, 1969, **2**, 279.

SIR,—The opportunity for clinicians to communicate their clinical interpretation of the cause of death (14 October, p 1063) to the coroner via the pathologist is already freely available at the time of necropsy. How many take the opportunity, or even fill in a meaningful request form? Direct communication between the coroner and the clinician is unnecessary if the clinician attends the necropsy, and this saves his and the coroner's time.

The relatively good correlation between death certification and hospital notes in cases where no necropsy has been performed proves only that clinicians can interpret their notes, but little about the true cause of death. What might a necropsy have shown? The poor correlation where hospital necropsies have been done can only mean that clinicians do not understand the reports they receive, or have not attended the necropsy.

The interpretation of this study must be that clinicians should attend necropsies and talk to pathologists, and that the falling necropsy rate should be reversed.

T A FRENCH
P J H FLETCHER
B G OCKENDEN

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SIR,—The paper on death certification and epidemiological research (14 October, p 1063) appears to be misleading in several of its premises and conclusions, and it is disappointing to see it published in your journal at the same time as the excellent series of articles on epidemiology by Professor Geoffrey Rose and Dr D J P Barker.

In the discussion section it is rightly pointed out that the underlying cause of death

is taken as the last diagnosis under section I of the certificate; yet in tables II and III, purporting to demonstrate "major discrepancies" between recorded and "actual" cause of death, several examples appear where the underlying cause, so defined, is manifestly the same.

A more fundamental fault, however, lies in the implicit assumption that "actual" cause of death can be defined. The authors assume that the cause of death assigned by their consultant colleagues is always the true one, and those of the certifying doctors, coroners, and pathologists potentially erroneous. In the introduction reference is made to earlier papers, all of which have a different premise—namely, that the necropsy-supplied cause is the true one. What is being studied is, of course, another example of observer variation or bias, and it is fortuitous for the authors that this is explained clearly in the series by Rose and Barker to which they refer. The perplexed epidemiologist whom their paper presumably aims to assist will, of course, be well aware of this phenomenon. Meanwhile one can only recommend to the senior clinicians concerned that if they remain unconvinced that they too might err they should fill in the death certificate themselves.

D M PARKIN

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Acute stroke

SIR,—Hopefully the article by Dr Graham Mulley and his colleagues (7 October, p 994) will stop the use of dexamethasone in acute stroke. Hitherto, too many patients have been given too much dexamethasone for too long a period with the production of frightening side effects rather than benefit. It is good to see a useless treatment being debunked and perhaps this is an appropriate time to debunk a useless investigation—namely, the lumbar puncture. While in the trial situation, such as described by Dr Mulley, there may be a place for examining the cerebrospinal fluid, there is surely no justification for this procedure as a routine investigation. As 134 patients in one general hospital were admitted to this trial over a 13-month period, what a saving there would be on a national level if dexamethasone were not prescribed and lumbar punctures not performed.

A C YOUNG

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SIR,—The study reported by Dr Graham Mulley and others (7 October, p 994) seems to give a fairly definite answer, in the negative, to the question of whether or not the disability resulting from thrombotic stroke might be diminished by giving steroids. I should like to draw your attention to a similar study carried out under the auspices of the New Zealand Medical Research Council's Standing Committee on Therapeutic Trials. This study¹ used betamethasone instead of dexamethasone but in similar dosage and for the same period, although the number of cases suitable for analysis was smaller.

The results were even more discouraging than those of Dr Mulley and his colleagues, there being a significantly higher death rate among the betamethasone group than those treated with placebo injections. There would certainly not seem to be any indication for this

type of treatment in the generality of thrombotic strokes.

E G McQUEEN

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¹ McQueen, E G, *New Zealand Medical Journal*, 1978, **87**, 103.

Maprotiline hydrochloride and grand-mal seizures

SIR,—We thought it would be helpful to doctors if we commented on the letter from Drs M J Hall and R I Russell (30 September, p 961) describing a patient who had a grand-mal seizure when taking maprotiline (Ludiomil).

Of course it is well known that tricyclic antidepressants as well as tetracyclic compounds can cause epileptic seizures in some patients.¹⁻³ While it is true that we have little knowledge of the exact incidence of seizures in patients taking maprotiline, this is also true of other antidepressant drugs which have been on the market for much longer. The whole subject was well reviewed recently by Trimble,⁴ who regards maprotiline, along with flupenthixol, viloxazine and nomifensine, as least likely to excite epilepsy in known epileptic patients. It is, of course, difficult to obtain entirely reliable data on the exact incidence of a side effect when the number of cases seen by one investigator is very small.

The dosage recommendation for Ludiomil is normally 25-150 mg daily (*Data Sheet Compendium*, 1978), and we would like to emphasise that higher doses are required only in exceptional cases. This is important because epileptic seizures are rare when the dose is below 150 mg. The patient described had her dose of maprotiline quadrupled to 300 mg and was also taking Ovranette, which could increase susceptibility to epilepsy if there was fluid retention (*Data Sheet Compendium*, 1978). Also, several years ago Mills⁵ advised the prescription of an anticonvulsant to any patient taking over 200 mg of a tricyclic antidepressant.

Be assured that we will continue to define, by studies currently under way, the epileptic potential of Ludiomil in the hope of advising doctors even better how to use the drug safely.

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¹ Betts, T A, *et al*, *Lancet*, 1968, **1**, 390.

² Dallos, V, and Heathfield, K, *British Medical Journal*, 1969, **4**, 80.

³ Escande, M, *et al*, *Encephale*, 1976, **11**, 133.

⁴ Trimble, M, *Epilepsia*, 1978, **19**, 241.

⁵ Mills, I H, *Practitioner*, 1976, **217**, 529.

Abnormal cerebrovascular regulation in hypertensive patients

SIR,—Dr D N W Griffith and others (9 September, p 740) report on a defective carbon dioxide (CO₂) response in the cerebral circulation of 10 middle-aged hypertensive patients. In a similar study published in 1976¹ we found essentially no difference in cerebrovascular CO₂ response between hypertensive and normotensive patients. The authors

suggest that this discrepancy may be due to our Japanese patients having "concomitant medical problems" or "taking various medications"—leading surprisingly to a normal CO₂ response. To explain their own observations Dr Griffith and his colleagues suggest a functional disorder of the brain vessels in their hypertensive patients.

Inhalation of CO₂ in acute experimental hypertension causes an extreme rise in cerebral blood flow (CBF).² The finding of a normal rise in CBF in a hypertensive patient during CO₂ inhalation signifies structural and functional adaptation of the resistance vessels to the hypertensive state. This is analogous to the adaptation of CBF autoregulation to high blood pressure demonstrated in hypertensive patients.³ The finding of a decreased response or even a decrease in CBF during CO₂ inhalation, on the other hand, may be caused by stenosing atherosclerosis of the major brain vessels. Thus experimental carotid occlusion in the baboon diminishes the rise in CBF caused by CO₂ inhalation by exhausting the arteriolar dilatatory capacity in the resting state.⁴

Our Japanese patients had bilateral carotid angiography as part of their clinical investigation and were included in the CO₂ reactivity study only if no significant cerebral atherosclerosis or other abnormality was present. Further, they were as a group somewhat younger than the patients of Dr Griffith and his colleagues (mean age 43 v 50 years), who were not investigated for atherosclerosis. It may also be mentioned that the extracerebral compartment of CBF, as measured by the ¹³³Xe-inhalation method used by them, would be expected to decrease during CO₂ inhalation. Hypercapnia causes a generalised vasoconstriction (and thereby a rise in blood pressure) and has a dilatatory effect only in limited areas such as the cerebral and coronary circulations.

In conclusion, the discrepancy between the results of Dr Griffith and his colleagues and our own may be due to more pronounced atherosclerosis in the British hypertensive patients or it may be due to differences in methodology.

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¹ Tominaga, S, *et al*, *Stroke*, 1976, **7**, 507.

² Ekström-Jodal, B, *et al*, *European Neurology*, 1971, **6**, 6.

³ Strandgaard, S, *et al*, *British Medical Journal*, 1973, **1**, 507.

⁴ Sengupta, D, *et al*, *Journal of Neurology, Neurosurgery and Psychiatry*, 1973, **36**, 736.

Spinal cord transection in utero

SIR,—Dr I Blumenthal's letter (16 September, p 835) concerning our case report "Spinal cord transection in utero" states that a similar case has been reported from Japan recently. We wish to point out that the paper quoted by him described a case of a breech presentation with marked hyperextension of the neck, where despite delivery by caesarean section the baby suffered spinal cord damage. This damage must be presumed to have occurred at birth, since the baby was completely flaccid for some time after birth and only later developed spasticity.

The point of our case report was that the spinal cord damage must have occurred some weeks prior to birth, probably caused by external cephalic version.

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Cost-effectiveness studies

SIR,—In your leading article (23 September, p 848) you state that "in many other cases the [cost-effectiveness] analysis can contribute little to any debate." The example you choose to illustrate this point is elective hysterectomy. Bunker *et al*¹ provide evidence of a small improvement in life expectancy but little evidence of changes in quality of life. Thus the evidence for or against the procedure is inconclusive. But it cannot be concluded because the evidence is not convincing in this way that the analysis contributes little to the debate. Quite the contrary—no individual or community would be wise to devote resources to procedures which have little or no demonstrable benefit (though, of course, they do). Where society is concerned Bunker and his colleague come to the same conclusion, that "at issue will be the allocation of public funds for a procedure where it appears to be more of a convenience or a luxury than a necessity . . . in competition . . . with other medical procedures, many of which may present stronger claims."

The economist's function in cost-benefit analysis is to try to highlight the implications of following one procedure rather than another. The alternative procedure may often be doing nothing. As both economists and doctors as a profession are interventionists inaction tends to be unacceptable. So, to return to the example of hysterectomy, it might be said that cost-benefit analysis contributes little to the debate because it indicates that non-intervention appears to be almost as beneficial as intervention.

Economists also believe in consumer sovereignty and therefore one might ask what most women would choose if presented with the choice of elective hysterectomy or the money cost of the procedure.

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University of Exeter

¹ Bunker, J P, *et al* (editors), *Costs, Risks and Benefits of Surgery*. New York, Oxford University Press, 1977.

Expanding role for pharmacists

SIR,—Your leading article (30 September, p 911) on an expanding role for pharmacists in medical care will be welcomed in schools of pharmacy and in the pharmaceutical profession at large as a sign of encouragement to those seeking to change the emphasis of the work of the pharmacist.

There is certainly no disagreement among those who seek more clinical involvement by the pharmacist that the physician has the ultimate responsibility for the care of the patient, nor is there any ambiguity about the role of the physician and the clinical pharmacist, for the training of both approaches the topic of medication from different directions. The physician is largely clinically trained and the pharmacist scientifically trained. The com-

plexity of modern medication dictates that no one person, physician or pharmacist, can be aware of all aspects of drug therapy. Nevertheless, there is frequently encountered medical resistance to advice proffered by pharmacists. To ensure that standards of therapy are improved surely it is important that physicians consult and listen to those with a training relevant to the use of drugs and to patient care.

It may be that resistance to pharmacists is still evident because there is little understanding of the training of the modern pharmacy graduate. Your readers may be unaware that there have been marked changes in the education of pharmacists in the last few years. Some of these changes are indicated by the appointment of a physician as a professor of clinical and community pharmacy at one of our universities. In my own university we have a consultant pharmacologist as visiting professor to the school of pharmaceutical sciences and my own department has a visiting teaching fellow who is both medically and pharmaceutically qualified. A scheme of clinical training was introduced last year for some of our final-year undergraduates. Several schools now offer master's degrees in clinical pharmacy.¹ The master's course in clinical pharmacy at the University of Strathclyde is typical of several courses. It covers in its first year drug metabolism, distribution, and excretion; pathology in relation to clinical pharmacy; and techniques in clinical pharmacology. In the second year the subjects covered include evaluation, safety, and control of medicines; practice of clinical pharmacy; pharmacokinetic workshops; and a research project. Courses such as ours are pursued by honours graduates in pharmacy after a year of preregistration training, so that pharmacists holding a master's degree in clinical pharmacy have at least six years (seven years in Scotland) of intensive training behind them. The formal course is largely taught by members of staff of the school but supplemented by clinical visits and seminars with over 30 clinicians. We feel that we are making the correct moves and await some reciprocation from medical faculties to involve us more in the training of doctors.

Your continued support in encouraging physicians to employ the undoubted skills of pharmacists usefully must eventually have the effect of improving patient care. It has nothing whatsoever to do with pharmaceutical aggrandisement.

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¹ Florence, A T, *Journal of Clinical Pharmacy*, 1977, **2**, 119.

SIR,—I read with great interest your leading article "Expanding role for pharmacists" (30 September, p 911). It is gratifying that you should print so many truths without a hint of the anti-doctor, anti-pharmacist sniping which has grown over recent years.

There is no doubt that the pharmacist would be of much greater assistance to his medical colleague if his course had a greater clinical content but even now there is so much unused potential. Pharmacists now supply good independent drug information in assimilable form without bias, are able to supply quality test results, and generally contribute to safer prescribing. Their help is particularly needed in psychiatric and geriatric prescribing because